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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/138,735	08/24/1998	GLAUCIA PARANHOS-BACCALA	WPB-36400B	4465

25944 7590 03/21/2002

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EXAMINER	
GRASER, JENNIFER E	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 03/21/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/138,735	Paranhos-Baccala et al.
Examiner	**Art Unit**
Jennifer Graser	1645

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *Request for CPA & Pre. Amendt. F* .

2a)☐ This action is **FINAL.** 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1, 2, 5, 7, 8, 10-27, 32, 34, and 36-40* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1 and 2* is/are allowed.

6)☒ Claim(s) *5, 7, 8, 10-27, 32, 34, and 36-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some* c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☐ Notice of References Cited (PTO-892)

16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18)☐ Interview Summary (PTO-413) Paper No(s). _____

19)☐ Notice of Informal Patent Application (PTO-152)

20)☐ Other:

DETAILED ACTION

Continued Prosecution Application

1. The request filed on 1/24/02 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/138,735 is acceptable and a CPA has been established. An action on the CPA follows.

Acknowledgment and entry of the Preliminary Amendment submitted 1/24/02, Paper No. 18/F is made. Claims 1, 2, 5, 7, 8, 10-27, 32, 34 and 36-40 are currently pending.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 5, 7, 8, 10-27, 32, 34 and 36-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 5 and 8 are vague and confusing because it recites a probe[primer] which has at least 85% homology with a fragment of a nucleotide sequence that is identical or fully complementary to nucleotides 1232-2207 of SEQ ID No:1 or the corresponding RNA sequence, where said probe contains at least 5 and no more than 100 nucleotides. Do Applicants intend for the claim to read on a 5 nucleotide length probe[primer] which has 85% homology to nucleotides 1232-2207 of SEQ ID NO:1 or do they intend to encompass a 5 nucleotide probe[primer] *which*

*is derived from a fragment which is 85% homologous to nucleotides 1232-2207 of SEQ ID NO:*1? The claims currently include the scope of the latter which allows for probes[primers] which have not yet been identified by Applicant, i.e., if derived from the 15% of the non-homologous portion. Clarification is requested.

Claim 10 is dependent on a cancelled claim, i.e., claim 9. Correction is requested.

Claims 18, 19 and 27 are vague and indefinite because it fails to state the hybridization conditions. As previously set forth, hybridization parameters can vary considerably. A number of parameters govern the stringency of the hybridization including the hybridization time, hybridization temperature, washing temperature, washing time, formamide concentration, detergent concentration and salt concentration. Changes in these parameters will affect the specificity of any given probe. Thus, in order to ascertain the metes and bounds of the claim, the skilled artisan would require a knowledge of these parameters. The claim amendments fail to address this deficiency and do not clearly and unambiguously set forth the appropriate reaction conditions. While the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims. The claims as they stand are incomplete and fail to provide adequate structural properties to allow for one to identify what is being claimed. The rejection may be obviated by clearly setting forth the reaction conditions encompassed, as supported by the disclosure.

Claims 21-23 are vague and indefinite because they recite a nucleotide sequence which is 85% homologous to a sequence which is identical or fully complementary to sequence 1232[1266]-1825[2207] of SEQ ID NO:1 or the corresponding RNA sequence, wherein each segment of 30 contiguous nucleotides has at least 85% homology with a segment of 30 contiguous nucleotides of said reference sequence; however, it is unclear how large this sequence is. Further, are the 30 contiguous sequences each backed up one to another, are they spaced apart? The language of this claims is extremely vague and confusing. Accordingly, the metes and bound cannot be understood.

Claims 36-38 lack antecedent basis for "said nucleotide sequence (a)". There is no "(a)" in claims 21-23. Appropriate correction is required.

Claim Rejections - 35 USC § 112-New Matter

4. Claims 5, 7, 8, 11-20, 25, 26, 32, 34, and 36-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Support for the limitation, "wherein said primer[probe] comprises a nucleotide sequence having at least 85% homology with a fragment of a nucleotide sequence that is identical or fully complementary to a sequence starting at 1232/1266 and ending at 1825/2207 of SEQ ID NO:1 or the corresponding RNA sequence, wherein said probe/primer contains at least 5....." or for "a fragment that comprises a nucleotide sequence having at least 85%

homology with a reference sequence that is identical or fully complementary to a sequence starting at 1232 and ending at 2207 of SEQ ID NO:1 or the corresponding RNA sequence..." could not be found in the instant specification. The specification only refers to percent homology to the full-length sequence of SEQ ID NO:1 and does not specifically recite probes or primers with a specified homology to the specified fragments recited in the instant claims. See page 4, lines 23-32 and page 15, lines 15-33, which does not provide support for the claim language as it only recites homology to full-length sequence of SEQ ID NO:1 and not to the specific fragments recited in the claims.

However, support for claims 21-23 is found on page 7, lines 15-19 and in the originally filed claims. Support could also not be found for "degenerates" as recited in newly submitted claims 36-38. When providing a new limitation, Applicant should point out to the specific section of the specification by page and line number which provides support for the new limitation.

Claim Rejections - 35 USC § 112-Enablement

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 5, 7, 8, 10-27, 32, 34 and 36-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The breadth of the instant claims contain nucleotide sequences other than what is specified in the sequence disclosure. The specification states that substitutions, additions, or deletions may be made to the defined sequences; however, the specification provides no guidance as to what nucleotides may be changed without causing a detrimental effect to the protein to be produced or its ability to function as a probe or primer. Further, it is unpredictable as to which nucleotides could be removed and which could be added. Claims 5 and 8 recite a probe[primer] which has at least 85% homology with a fragment of a nucleotide sequence that is identical or fully complementary to nucleotides 1232-2207 of SEQ ID No:1 or the corresponding RNA sequence, where said probe contains at least 5 and no more than 100 nucleotides. These clams encompass a 5 nucleotide probe[primer] *which is derived from a fragment which is 85% homologous to nucleotides 1232-2207 of SEQ ID NO:*1. The claims currently include the scope of the latter which allows for probes[primers] which have not yet been identified by Applicant, i.e., if derived from the 15% of the non-homologous portion. Accordingly, it would take one of skill in the art undue experimentation to make and/or use these probes/primers. Further, it is unclear that such a probe or primer, one that does not have sequence homology to the reference sequence, would have the ability to identify/amplify a T.cruzi sequence. Claims 21, 22 and 23 recite sequences which are 85% homologous to 30 contiguous monomers. This allows for a great deal of difference from that which is disclosed in the specification, i.e., much more than

85% variance. These sequences would be up to 70-95% different from SEQ ID NO:1. Sequences with this much deviation would not be able to function as probes or primers. It is unclear what sequence this encompasses and what function it would serve. The breadth of the instant claims contain nucleotide sequences other than what is specified in the sequence disclosure. The specification states that substitutions, additions, or deletions may be made to the defined sequences; however, the specification provides no guidance as to what nucleotides may be changed without causing a detrimental effect to the probe or primer to be produced. Additionally, 18, 19, 20, 24, 27, 29 and 31-35 are also not enabled as they fail to recite the specific hybridization conditions to be used in the methods. Low stringency conditions would not allow for a successful assay. Applicants have provide no guidance to enable one of ordinary skill in the art how to determine, without undue experimentation, the effects of different nucleotide substitutions and the nature and extent of the changes that can be made. Given the lack of guidance contained in the specification and the unpredictability for determining acceptable nucleotide substitutions, one of skill in the art could not make or use the broadly claimed invention without undue experimentation.

Response to Applicants' Arguments:

Applicants argue that one of ordinary skill in the art would be able to determine appropriate sequences by merely routine experimentation for various purposes, such as serving as probes and primers. This has been fully and carefully considered but is not deemed persuasive.

Claims 5 and 8 read on probes and primers which do not contain any of the nucleotides recited in SEQ ID NO:1, i.e., they may be derived from a sequence with 85% homology to portions of SEQ ID NO:1. A 5 nucleotide probe/primer derived from this 85% homologous sequence can contain 5 nucleotides from the 15% region which is different from SEQ ID NO:1. Sequences with this much deviation would not be able to function as probes or primers. It is unclear what sequence this encompasses and what function it would serve. The breadth of the instant claims contain nucleotide sequences other than what is specified in the sequence disclosure.

Claim Rejections - 35 USC § 112- Written description

7. Claims 5, 7, 8, 10-27, 32, 34 and 36-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description in this case only sets forth SEQ ID NO:1, SEQ ID NO: 1 (1232-1825), SEQ ID NO:1 (1232-2207) and equivalent degenerative codon sequences thereof and therefore the written description is not commensurate in scope with the claims drawn to sequences which are 85% homologous to a 30 nucleotide segment and fragments which contain sequences which are complementary to sequences which are antisense which are 5 and 8 nucleotides in length, etc.. or to probes and primers which do not contain any of the nucleotides recited in SEQ ID NO:1, i.e., they may be derived from a sequence with 85% homology to

portions of SEQ ID NO:1 (claims 5 and 8). A 5 nucleotide probe/primer derived from this 85% homologous sequence can contain 5 nucleotides from the 15% region which is different from SEQ ID NO:1.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Reiger et al (Glossary of Genetics and Cytogenetics, Classical and Molecular, 4th Ed., Springer-Verlay, Berlin, 1976) clearly define alleles as one of two or more alternative forms of a gene occupying the same locus on a particular chromosome..... and differing from other alleles of that locus at one or more mutational sites (page 17). Thus, the structure of naturally occurring allelic sequences are not defined. With the exception of SEQ ID NO:1, the skilled artisan cannot envision the detailed structure of the encompassed polynucleotides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic

acid itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Support for antisense and sequences and fragments of varying percent identity is stated. However, no disclosure, beyond the mere mention of these potential sequences is made in the specification. This is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Therefore only an isolated DNA molecule comprising a DNA sequence consisting of nucleotides 1232-1825, 1232-2207 of SEQ ID NO:1 or SEQ ID NO:1 and equivalent degenerative codon sequences thereof, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph.

Response to Applicants' Arguments:

Applicants argue that a high degree of homology has been claimed (85%) with respect to a defined sequence. They argue that the inventors clearly contemplated such sequences. Applicants further argue that literal support is not needed if the disclosure of the application conveys to the artisan that the inventor had possession at the time of the claimed subject matter. These arguments have been fully and carefully considered but are not deemed persuasive.

Claims 5 and 8 encompass probes and primers which do not contain any of the nucleotides recited in SEQ ID NO:1, i.e., they may be derived from a sequence with 85% homology to portions of SEQ ID NO:1. A 5 nucleotide probe/primer derived from this 85% homologous sequence can contain 5 nucleotides from the 15% region which is different from SEQ ID NO:1. Claims 21, 22 and 23 recite sequences which are 85% homologous to 30 contiguous monomers. This allows for a great deal of difference from that which is disclosed in the specification, i.e., much more than 85% variance. These sequences would be up to 70-**95%** different from SEQ ID NO:1. Conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it.

8. Claims 1 and 2 are allowed.

9. Correspondence regarding this application should be directed to Group Art Unit 1645. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The

faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is (703) 308-4242 which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (703) 308-1742. The examiner can normally be reached on Monday-Friday from 7:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

J Graser 3/29/02

Jennifer Graser
Primary Examiner
Art Unit 1645